present invention are useful in the diagnosis of unstable angina and myocardial infarction.

Claims 1 and 55-133 are pending in the instant application, and claims 85-96, 102-106, and 114-133 are currently under consideration by the Examiner, claims 1, 55-84, 97-101, and 107-113 having been withdrawn from consideration by Restriction Requirement. Applicants have cancelled claims 1, 55-84, 97-101, and 107-113, amended claims 85, 88, 91, 94, and 102, and added new claims 134-142 herein.

The new and amended claims are fully supported by the specification and do not introduce new matter or require a new search. Support for using antibody cocktails in assays is provided in the specification, *e.g.*, on page 24, lines 21-29. The amended claims simply clarify the claimed subject matter using preferred terminology, and are commensurate with or enlarge the scope of the previously pending claims. For example, the amendment to claim 85 merely clarifies the meaning of the phrase "and/or" originally in the claim; and the amendment to claim 102 clarifies that "any cardiac specific troponin isoform" refers to cardiac specific troponin I and cardiac specific troponin T.

Notwithstanding the foregoing, Applicants expressly reserve the right to pursue subject matter no longer claimed in the instant application in one or more applications which may claim priority hereto. Applicants respectfully request reconsideration of the claimed invention in view of the foregoing amendments and the following remarks.

Non Art-Related Remarks

Oath/Declaration

The Examiner has objected to the declaration filed with the instant application, stating that it is defective for failing to identify the post office address of each inventor. Applicants respectfully submit that the combined declaration and power of attorney submitted with the divisional application on July 7, 1999 provides the address of each inventor, and, therefore, request clarification of the Examiners objection in this regard.

Abstract of the Disclosure

The Examiner referred Applicants to the proper language and format for an abstract of the disclosure. Applicants gratefully acknowledge the referral, and submit that the foregoing amendments to the specification provide an acceptable abstract.

35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 85 under 35 U.S.C. § 112, second paragraph, contending that the phrase "and/or" renders the claim indefinite, and that it is unclear how signal production is effected in the absence of a label. With respect to the phrase "and/or," Applicants believe that the foregoing claim amendments render this rejection moot. With respect to how signal production is effected in the claims, Applicants respectfully traverse this rejection.

When determining definiteness, the proper standard to be applied is "whether one skilled in the art would understand the bounds of the claim when read in the light of the specification." *Credle v. Bond*, 30 USPQ2d 1911, 1919 (Fed. Cir. 1994). See also *Miles Laboratories, Inc. v. Shandon, Inc.*, 27 USPQ2d 1123, 1127 (Fed. Cir. 1993) ("If the claims read in the light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.") (emphasis added).

Methods for performing immunoassays to detect the presence or amount of an analyte, for example, sandwich immunoassays and competitive immunoassays, are well known in the art. "A patent need not disclose what is well known in the art." *In re Wands*, 858 F.2d 731, 735, 1988. Methods using at least one labeled reagent represent preferred embodiments for practicing the claimed invention, however, the claimed invention is not limited to only those embodiments using a labeled reagent. For example, an assay may use a biosensor which directly detects antibody/antigen binding. Similarly, an assay may directly detect binding of an analyte to an antibody, for example using direct optical methods such as those disclosed in U.S. Patent No. 5,418,136. Thus, with respect to how signal production is effected in the claims, the ordinarily skilled artisan is reasonably apprised of the scope of the claims.

Therefore, because claim 85 meets the standard of 35 U.S.C. § 112, second paragraph, Applicants request that the Examiner withdraw this rejection.

The Examiner has also rejected dependent claims 86, 87, 89, 90, 92, 93, 95, 96, 103-106, 115-118, 120-123, 125-128, and 130-133, contending that the use of the indefinite article "an" results in improper antecedent basis, and that the claims must be amended to use the definite article "the." Applicants respectfully traverse this rejection.

The use of an indefinite article in a dependent claim is acceptable under current practice. *See, e.g.*, MPEP § 608.01(n)(I)(A). Furthermore, there is nothing of record to indicate that the language renders the claim unclear. Thus, because the ordinarily skilled artisan is fully apprised of the scope of the rejected claims, the standard of 35 U.S.C. § 112, second paragraph, has been met. *See, e.g.*, MPEP § 2173.05(e). Applicants, therefore, request that the Examiner withdraw this rejection.

The Examiner has also rejected claim 102, contending that the phrase "any" renders the claim indefinite. Applicants submit that the foregoing claim amendments render this rejection moot.

The Examiner has also rejected claim 104, contending that the phrase "approximately equal" is indefinite. Applicants respectfully traverse this rejection.

The use of relative terminology, such as the term "approximately," does not automatically render a claim indefinite under 35 U.S.C. § 112, second paragraph. As stated in *Andrew Corp. v. Gabriel Electronics, Inc.*, 6 USPQ2d 2010, 2012 (Fed. Cir. 1988), such words are "ubiquitous in patent claims. Such usages, when serving reasonably to describe the claimed subject matter to those of skill in the field of the invention... have been accepted in patent examination and upheld by the courts." Moreover, as discussed above, the test for definiteness requires only that the claims define the patented subject matter with a reasonable degree of clarity.

Here, the term "approximately" is well known to the ordinarily skilled artisan as meaning "nearly exact." Thus, the artisan would understand that two assay signals are

"approximately equal" when the signals are nearly exactly equal. This determination can be easily made by comparing the value of the two signals. Furthermore, while the Examiner contends that "the specification does not provide a standard for ascertaining the requisite degree" of equality required (Paper No. 9, page 5), this is incorrect. For example, on page 11, lines 27-30, the instant specification states that such an assay "will yield an assay response that is the same, within about a factor of two and preferably within 20%, for each form of troponin."

Accordingly, because the ordinarily skilled artisan would be reasonably apprised of the scope of the claims regarding the phrase "approximately equal," Applicants respectfully submit that the claim meets the standard of 35 U.S.C. § 112, second paragraph, and request that the Examiner withdraw this rejection.

Art-Related Remarks

35 U.S.C. § 102

The Examiner has rejected claims 102-103, 114-115, 119-120, and 124-125 under 35 U.S.C. § 102(b) as allegedly being anticipated by Bodor *et al.*, Clinical Chemistry 38: 2203 (1992). Applicants respectfully traverse this rejection.

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the specification. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990); *see also* MPEP § 2131.

The instant claims describe assay methods that comprise performing an assay with antibody that specifically binds to one or more free and complexed cardiac specific troponin isoforms. For example, claims 102 and 103 describe performing an assay with antibody that specifically binds free and complexed cardiac specific troponin I, and free and complexed cardiac specific troponin T. Similarly, claims 114, 115, 119, 120, 124, and 125 each describe performing an assay with antibody that specifically binds to both a free and a complexed cardiac specific troponin isoform.

The Examiner contends that the Bodor *et al.* reference discloses an assay for a cardiac specific troponin isoform, and also discloses two antibodies (3C5.10 and 1E11.3) that specifically bind only free cardiac troponin I, and another antibody (5D4.1) specific for the troponin I/C binary complex. Paper No. 9, page 6.

However, only the 1E11.3 antibody is specific for cardiac troponin, as required by the instant claims. Unlike the antibodies of the instantly claimed methods, the other antibodies (3C5.10 and 5D4.1) are not specific to cardiac troponin I, but instead bind both cardiac and skeletal troponin I. (Bodor *et al.*, Table 1). Moreover, the Examiner admits that 1E11.3 is specific for only free, and not complexed troponin I, and the Bodor *et al.* reference does not disclose pooling any of these antibodies for use in a single assay, in order to provide an antibody that binds to both free and complexed cardiac specific troponin isoforms, as required by the instant claims. Finally, the Bodor *et al.* reference discloses no antibodies that specifically bind free troponin T, or that specifically bind troponin T present in a complex.

Accordingly, because the Bodor *et al.* reference does not provide each and every element of the instant claims, no *prima facie* case of anticipation has been established. Applicants, therefore, request that the Examiner withdraw this rejection.

35 U.S.C. § 103

The Examiner has rejected claims 85-93, 104-106, 116-118, 121-123, and 126-128 under 35 U.S.C. § 103(a) as allegedly being obvious in view of Bodor *et al.*, and claims 94-96 and 129-133 as allegedly being obvious in view of Katus *et al.*, Clinical Chemistry 38: 386 (1992), in further view of Bodor *et al.* Applicants respectfully traverse these rejection.

To establish a prima facie case of obviousness, three criteria must be met: there must be some motivation or suggestion, either in the cited references or in knowledge available to one skilled in the art, to modify or combine the cited references; there must be a reasonable expectation of success in combining the references to achieve the claimed

invention; and the references must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2143.

As discussed above, the Bodor *et al.* reference does not disclose any antibodies that specifically bind any cardiac specific complexed troponin isoforms, or pooling antibodies to provide an antibody that bind both free and complexed troponin isoforms, as required by the instant claims. Moreover, the skilled artisan would not be motivated to provide such an antibody, because there is no suggestion in the Bodor *et al.* reference that measurement of both free cardiac specific troponin isoforms, together with complexes comprising such isoforms, is required or advantageous in order to obtain an accurate measure of cardiac troponin in patient samples. *See* specification, page 18, lines 23-32. Thus, the Bodor *et al.* reference fails to teach or suggest all the limitations of the instant claims. *See* MPEP § 2143.03.

Additionally, the Examiner contends that "Bodor specifically taught that dependency of binding on the existence of an antigen in a complex form opens up possibilities for investigating complex interactions" (Paper No. 9, page 10, emphasis added). This is an incorrect statement. The Bodor *et al.* reference actually states that "[t]his TnC-dependent mAb opens up possibilities for investigating TnI-TnC interactions," and not complex interactions generally. For example, there is no suggestion that such an antibody would be useful for ternary complexes.

Moreover, this statement is, at best, a mere invitation to experiment, creating an "obvious to try" situation that cannot support a *prima facie* case of obviousness. *See, e.g.*, *In re Eli Lilly & Co.*, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990) ("An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.") *See also In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (defining obvious-to-try as when prior art gives "only general guidance as to the particular form of the claimed invention or how to achieve it").

In the instant case, the results that the skilled artisan could expect from the investigations suggested by the Examiner were entirely unpredictable, and did not suggest that antibodies that specifically bind to such complexes would be necessary to provide an accurate measure of a troponin isoform in patient samples. Thus, there is no suggestion to provide antibodies that bind to both free and complexed cardiac specific troponin isoforms, as required by the instant claims, for use in a single assay. There is no motivation to one skilled in the art, other than that provided by the applicant's disclosure, to modify the reagents of the Bodor *et al.* reference to produce the claimed assay methods. *See* MPEP § 2143.

Furthermore, the Bodor *et al.* reference teaches away from assays which determine the presence or amount of cardiac specific troponin isoforms which are present in complexes. While the 5D4.1 antibody recognized the troponin I/C binary complex (Bodor *et al.*, page 2207), this antibody was excluded from use in assays used to assess the value of a cardiac troponin I assay (page 2208). This exclusion would suggest to one skilled in the art that antibodies specific to troponin complexes are not necessary for assessing patient samples, thus discouraging their use.

Moreover, the Katus *et al.* reference cited by the Examiner does not cure the deficiencies of the Bodor *et al.* reference. The Examiner contends that the Katus *et al.* reference discloses an assay for cardiac troponin T, but admits that the Katus *et al.* reference fails to disclose any assay using an antibody that specifically binds to complexed cardiac troponin T. For this, the Examiner continues the faulty reliance on Bodor *et al.* As discussed above, however, there is no disclosure or suggestion, in the cited references, alone or in combination, to provide antibodies that bind to both free and complexed cardiac specific troponin isoforms, as required by the instant claims, for use in a single assay.

Therefore, because the cited references fail to teach or suggest all the claim limitations, and because there is no suggestion in the prior art to modify or combine the cited references, the Examiner has failed to establish a *prima facie* case of obviousness. Applicants, therefore, request that the Examiner withdraw these rejections.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the address and telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,

BROBECK, PHLEGER & HARRISON LLP

Dated: January 4, 2001

By: _____
Michael Whittaker
Registration No. 46,230

Brobeck, Phleger & Harrison LLP
12390 El Camino Real
San Diego, CA 92130
Telephone: (858) 720-2500
Facsimile: (858) 720-2555